
Development of Monoclonal Antibody Products Targeting SARS-CoV-2 for Emergency Use Authorization Guidance for Industry

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(2). Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)**

**December 2023
Clinical/Medical**

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TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	BACKGROUND	3
III.	DISCUSSION	4
A.	Criteria for the Issuance of an EUA	4
B.	Guiding Principles	4
C.	Development Program Considerations to Support Use Under an EUA	5
1.	<i>Chemistry, Manufacturing, and Controls</i>	<i>5</i>
2.	<i>Pharmacology/Toxicology</i>	<i>8</i>
3.	<i>Virology</i>	<i>9</i>
4.	<i>Clinical</i>	<i>11</i>

Development of Monoclonal Antibody Products Targeting SARS-CoV-2 for Emergency Use Authorization Guidance for Industry¹

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or office responsible for this guidance as listed on the title page.

I. INTRODUCTION

FDA is issuing this guidance to provide recommendations to sponsors on the development of monoclonal antibody (mAb) products targeting SARS-CoV-2 intended for the prevention or treatment of COVID-19, including recommendations on addressing the impact of emerging variants.

In February 2021, FDA published the guidance for industry *Development of Monoclonal Antibody Products Targeting SARS-CoV-2, Including Addressing the Impact of Emerging Variants, During the COVID-19 Public Health Emergency* (February 2021). The guidance was published as part of the Agency's efforts to facilitate the development and availability of COVID-19 therapeutics for the duration of the COVID-19 public health emergency (PHE), as declared under section 319 of the Public Health Service Act (PHS Act). In the Federal Register of March 13, 2023 (88 FR 15417), FDA listed certain COVID-19-related guidance documents that FDA was revising to continue in effect for 180 days after the expiration of the COVID-19 PHE declaration on May 11, 2023, during which time FDA planned to further revise the guidances. The February 2021 guidance on development of monoclonal antibody products targeting SARS-CoV-2 was included in this list.

On February 4, 2020, as amended on March 15, 2023, pursuant to section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic (FD&C) Act, the Secretary of Health and Human Services (HHS) has determined that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that the public health

¹ This guidance has been prepared by the Office of New Drugs and Office of Pharmaceutical Quality in the Center for Drug Evaluation and Research at the Food and Drug Administration.

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emergency involves the virus that causes COVID-19.² On the basis of such determination, the Secretary of HHS has declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564 of the FD&C Act, subject to terms of any authorization issued under that section.³ The HHS Secretary declaration authorizing FDA to issue emergency use authorizations (EUAs) is distinct from, and is not dependent on, an HHS public health emergency declaration under section 319 of the PHS Act. Although the PHE declaration under section 319 of the PHS Act has expired, the relevant EUA declaration under section 564 of the FD&C Act remains in effect.

Although circumstances have improved, SARS-CoV-2 remains in broad circulation throughout the United States. The virus has and continues to evolve over time, and in certain instances, mutations in the virus have greatly reduced the activity of monoclonal antibody therapies available for the prevention or treatment of COVID-19, resulting in vulnerable populations having limited preventative and treatment options. FDA is publishing this guidance to provide its current recommendations on the data and information that may be used to support a request for an EUA under section 564 of the FD&C Act (21 U.S.C. 360bbb-3) for a mAb product for the prevention or treatment of COVID-19. This guidance is intended to remain in effect only for the duration of the declaration by the Secretary of HHS under section 564 of the FD&C Act effective March 27, 2020, that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic (85 FR 18250).⁴

This guidance does not address the information and data necessary to support the licensure of mAb products under section 351 of the Public Health Service Act (42 U.S.C. 262).

Given the need to ensure that sponsors are aware of our current recommendations to facilitate timely development of monoclonal antibody products targeting SARS-CoV-2, FDA is issuing this guidance for immediate implementation without initially seeking prior comment because the Agency has determined that prior public participation is not feasible or appropriate (see 21 CFR 10.115(g)(2) and section 701(h)(1)(C)(i) of the FD&C Act (21 U.S.C. 371(h)(1)(C)(i))). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices. (see 21 CFR 10.115(g)(3)).

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of

² U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 360bbb-3*. February 4, 2020; (see 85 FR 7316 (Feb. 7, 2020)). U.S. Department of Health and Human Services, *Amended Determination of a Public Health Emergency or Significant Potential for a Public Health Emergency Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 360bbb-3(b)*. March 15, 2023; (see 88 FR 16644 (March 20, 2023) ("Amended Determination").

³ 85 FR 18250 (April 1, 2020). This Emergency Use Authorization declaration was effective March 27, 2020.

⁴ For more information about the determination and declaration under section 564 currently in effect, see *COVID-19 Emergency Use Authorization Declaration* (88 FR 16644 (March 20, 2023)).

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the word should in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

In 2019, an outbreak of respiratory disease caused by a novel coronavirus began. The virus was named “SARS-CoV-2,” and the disease it causes was named “Coronavirus Disease 2019” (COVID-19). Patients with symptomatic SARS-CoV-2 infection, or COVID-19, can experience a wide range of clinical manifestations, with disease severity ranging from mild to critical illness.⁵

The understanding of COVID-19 and its impact on public health has greatly increased since COVID-19 was first identified. Notably, during this time, FDA has authorized⁶ or approved a number of drugs and biologics for the prevention or treatment of COVID-19. However, SARS-CoV-2 has and continues to evolve, resulting in the emergence of multiple variants. A viral variant of SARS-CoV-2 has one or more mutations that differentiate it from the original Wuhan isolate (Wuhan-Hu1) or the predominant virus variant(s) already circulating in the general population. Variants of SARS-CoV-2 are identified by genomic sequences that contain mutation(s) in the RNA genome, which could result in amino acid substitutions, insertions, and/or deletions in viral proteins. Mutations in genomic regions encoding for viral proteins have been shown to negatively impact the expected therapeutic benefit of certain authorized drug products, particularly mAb products that bind to specific epitopes⁷ on the receptor binding domain of the SARS-CoV-2 spike protein.

Given this clinical context, FDA will continue to leverage its emergency authorities under section 564 of the FD&C Act, when appropriate. FDA may, in its discretion, prioritize requests for a mAb product containing sufficient scientific information to assess the known and potential benefits and risks of the product when there is no adequate, approved, and available alternative as such a product may address an unmet public health need.

It is FDA’s expectation that, following submission of an EUA request and issuance of an EUA, a sponsor would continue to collect data in any ongoing trials and would also work toward submission of a biologics license application as soon as possible.⁸

⁵ The different severities of COVID-19 illness are described in the National Institutes of Health (NIH) COVID-19 Treatment Guidelines at <https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/>.

⁶ More information about the availability of COVID-19 therapeutics under an EUA can be found at FDA’s Emergency Use Authorization web page, available at <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>.

⁷ For the purposes of this guidance, the term *epitope* refers to the part of an antigen, in this case the viral protein, to which an antibody binds.

⁸ FDA is required to periodically review the circumstances and appropriateness of an EUA, including the progress made toward licensure of a product. See section 564(g)(1) of the FD&C Act (21 U.S.C. 360bbb-3(g)(1)).

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III. DISCUSSION

A. Criteria for the Issuance of an EUA

- On February 4, 2020, as amended on March 15, 2023, pursuant to section 564(b)(1)(C) of the FD&C Act, the Secretary of HHS has determined that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that the public health emergency involves the virus that causes COVID-19.⁹ On the basis of such determination, the Secretary of HHS has declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564 of the FD&C Act, subject to terms of any authorization issued under that section.¹⁰
- Based on the above, FDA may issue an EUA for a drug or biological product after FDA has determined that the following statutory requirements are met (section 564(c) of the FD&C Act):
 - Based on the totality of scientific evidence available, including data from adequate and well-controlled trials, if available, it is reasonable to believe that:
 - The product may be effective to diagnose, prevent, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2.
 - The known and potential benefits of the product, when used to diagnose, prevent, or treat the identified serious or life-threatening disease or condition, outweigh the known and potential risks of the product.
 - There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition.¹¹

B. Guiding Principles

Sponsors of mAb products targeting SARS-CoV-2 should consider the following guiding principles:

⁹ See footnote 2.

¹⁰ See footnote 3.

¹¹ For example, a potential alternative product may be considered “unavailable” if there are insufficient supplies of the approved alternative to fully meet the emergency need. See section III., B., 1., d., of the guidance for industry *Emergency Use Authorization of Medical Products and Related Authorities* (January 2017). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

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- When scientifically supported, FDA will exercise flexibility regarding the data necessary to support the development of mAb products targeting SARS-CoV-2 and expedite the review of these data.
- An EUA is not a long-term alternative to obtaining licensure of a mAb product; therefore, sponsors should design their development programs with the goal of providing adequate data to ultimately support licensure of their products under section 351 of the Public Health Service Act.¹²
- In reviewing requests for EUA, FDA's approach will depend on, among other things, its current assessment of a mAb product's potential benefit and risk for the intended use and population and its expected coverage of important emerging variants.
- Given the rapid rate of SARS-CoV-2 viral evolution demonstrated and the relative vulnerability of some mAbs (e.g., mAbs targeting the receptor-binding domain (RBD)) to changing variants, FDA encourages the development of mAbs targeting highly conserved epitopes that have been relatively preserved over the course of the pandemic.
- FDA strongly recommends that individual mAb products (especially RBD-targeting mAbs) be developed with the expectation that they will be combined with one or more mAb products that bind to different epitopes to minimize the risk of losing activity against emergent variants. FDA encourages collaborations between sponsors of individual mAb products to achieve this end.
- Sharing of information regarding SARS-CoV-2 variants among sponsors, consortia, or other partnerships may help expedite the development of therapeutics to address these variants.

C. Development Program Considerations to Support Use Under an EUA

1. Chemistry, Manufacturing, and Controls

Sponsors of mAb products targeting SARS-CoV-2 should consider the following chemistry, manufacturing, and controls recommendations:

- When feasible and scientifically supported, sponsors should attempt to leverage experience obtained from other mAb products in development and already licensed mAb therapies. Specific examples include the following:
 - The use of existing manufacturing platforms to establish a manufacturing process for investigational product development.

¹² FDA is required to periodically review the circumstances and appropriateness of an EUA, including the progress made toward licensure of a product. See section 564(g)(1) of the FD&C Act (21 USC 360bbb-3(g)(1)).

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- The selection of manufacturing facilities¹³ that have experience in manufacturing biotechnology products and have an established inspectional history, including acceptable outcomes from recent inspection(s) (including using information shared by trusted foreign regulatory partners through mutual recognition agreements¹⁴).¹⁵
- The potential to use already obtained modular data for viral clearance validation, and a purification process validation (e.g., impurity clearance).
- The selection of analytical methods that have already been qualified or validated. The potency assay for a new mAb targeting SARS-CoV-2 spike protein should use the predominant circulating variant at that time. The potency assay¹⁶ formats (including binding assays and/or neutralizing assays) for a previous mAb may be adapted for the new mAb and should use revised reagents that evaluate the new variant protein(s) or pseudotyped virus/virus-like particles in the assay(s). Once a potency assay is established for release and stability testing of a specific anti-SARS-CoV-2 mAb, the assay does not need to be requalified or revalidated for use with new variants because the purpose of the assay is to ensure lot-to-lot consistency. However, the sponsor is expected to assess the mAb against newly arising variants to ensure that the product remains effective (see Virology section).
- The use of data that may be available from public consortia or partnerships that may contribute to understanding product performance.
- The leveraging of related product quality data (e.g., formulation development) to support in-use stability and compatibility.
- The use of prior development experience to anticipate the best dosage form, route of administration, and formulation (composition) selection.
- Sponsors that may not be able to leverage experience obtained from other mAb products in development or already licensed are also encouraged to develop mAbs against new SARS-CoV-2 variants. Specific options include the following:
 - Exploring opportunities for less experienced manufacturers to partner with more experienced manufacturers to leverage all available development tools

¹³ For information on facility recommendations pertaining to EUAs, see section III., D., 2., a., bullet 6 and section III., E., 5., a., of the guidance for industry and other stakeholders *Emergency Use Authorization of Medical Products and Related Authorities*.

¹⁴ See FDA's Mutual Recognition Agreement web page, available at <https://www.fda.gov/international-programs/international-arrangements/mutual-recognition-agreement-mra>.

¹⁵ See 21 CFR 601.20.

¹⁶ See the draft guidance for industry *Potency Assay Considerations for Monoclonal Antibodies and Other Therapeutic Proteins Targeting Viral Pathogens* (March 2023). When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

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- Exploring opportunities to partner with experienced manufacturers to use manufacturing facilities with inspection histories and mAb manufacturing experience
- Using publicly available prior knowledge related to upstream and downstream manufacturing processes for mAbs
- Using well-established cell substrates
- FDA strongly recommends that sponsors discuss with FDA in advance (well before they occur) time-critical elements of the development program. Specific examples include the following:
 - A plan that describes key aspects of the manufacturing development, including plans for scale-up, particularly if plans include use of facilities that do not have recent acceptable inspection history or experience manufacturing mAbs.
 - Comparability protocols that include a detailed description of tests and acceptance criteria to evaluate the impact of manufacturing process changes on product quality.
 - Plans to address shortages of raw materials for manufacturing or supplies for infusion of the mAb.
 - A strategy for establishing a shelf life for the intended mAb product targeting SARS-CoV-2. This may include opportunities to leverage related product data to justify the proposed shelf life.
 - Plans to meet predicted product demand.
- Certain approaches may be appropriate for limited early-phase development to enable rapid introduction of the product into clinical trials. Specific examples include the following:
 - Use of a stable cell pool in lieu of a clonally derived cell bank to generate early clinical batches. Risks of this approach include the ability to ensure comparability to products manufactured with a clonally derived cell bank. In addition, the upstream manufacturing process may require the use of antibiotics as selection reagents for more passages than would be needed when manufacturing using a clonally derived cell bank; therefore, clearance of antibiotics should be demonstrated and an evaluation of the permissible daily exposure should be provided.
 - Consideration of interim results from limited safety testing results (e.g., for cell banks, unprocessed bulk harvest) to begin first-in-human clinical trial(s) with full study reports to be available at time negotiated with FDA and submitted to the investigational new drug application (IND); however, when other therapies become available under EUA or through marketing approval, this limited safety testing may

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no longer be appropriate. Sponsors are encouraged to discuss the IND safety testing package in a pre-IND meeting with the review team.

- Flexibility in the amount of stability study results provided in the IND submission to support the initiation of first-in-human clinical trials.
- Use of two robust orthogonal virus clearance steps when modular/generic virus clearance data are not available.
- FDA may decide not to require completed process validation (excluding validation of the sterilization and aseptic processes for drug product) to support an EUA. However, sufficient process knowledge and/or characterization is expected and should be consistent with the overall benefit-risk assessment of the product. If only limited process validation data are provided, the sponsor can propose additional elements for the control strategy. These elements can include additional controls in the manufacturing processes, taking into consideration the criticality assessment for individual process parameters, the ranges proposed for a given parameter, or the inclusion of additional in-process measurements or release specifications.

2. *Pharmacology/Toxicology*

Sponsors of mAb products targeting SARS-CoV-2 should consider the following pharmacology/toxicology recommendations:

- The Agency intends to be flexible regarding nonclinical safety data expectations (e.g., content and/or timing of data submission to the IND) for mAb products targeting SARS-CoV-2 to support clinical trial initiation. The degree of flexibility warranted will be influenced by the risk characteristics of the product (e.g., original source and isotype of the mAb, nature of any amino acid changes/Fc domain modifications, manufacturing processes, product quality attributes), route of administration, potential coverage of important emerging variants, and a benefit-risk assessment for the intended trial population (e.g., hospitalized, nonhospitalized, healthy trial subjects). Thus, FDA strongly recommends that sponsors discuss the nonclinical safety data needed to support product administration in a specific clinical trial with the Agency through the pre-IND consultation process.
- Depending on the specific FDA recommendations provided during the pre-IND consultation process, the nonclinical safety assessment for mAb products targeting SARS-CoV-2 would typically follow approaches outlined in the ICH guidance for industry *S6(R1) Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals* (May 2012) and include the following:

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- A tissue cross-reactivity study using a panel of human tissues.¹⁷ When a mAb binds to human tissues in the tissue cross-reactivity study, FDA recommends evaluating mAb binding to select tissues from nonclinical species to assist in species selection for repeat-dose toxicology testing. When binding of potential clinical concern is observed (e.g., cell membrane binding), FDA recommends discussing these data with the Agency because additional studies may be needed to help inform the potential clinical relevance of the findings.
- A short duration (i.e., 3 weeks of treatment) repeat-dose toxicology study in a single species, using the clinical formulation and route of administration(s) intended for clinical administration, that includes all standard toxicity endpoints, including toxicokinetic analysis. FDA also recommends discussing specific study design considerations with the Agency.
- Toxicology studies with specific mAb combinations are not needed for mAb products targeting SARS-CoV-2 proteins, so mAb products can be evaluated separately in toxicology studies. If a sponsor evaluates mAb products in combination, FDA recommends using the same ratio intended for clinical administration.
- To support administration of mAb products during pregnancy, FDA recommends conducting a tissue cross-reactivity study using relevant human tissues or studies using alternative protein interaction technologies, with appropriate justification. If no specific concerns are identified in the toxicology studies, developmental and reproductive toxicology studies are not needed.

3. *Virology*

Sponsors of mAb products targeting SARS-CoV-2 should consider the following virology recommendations:

- A broad approach should initially be used to characterize the impact of amino acid changes, insertions, or deletions throughout the mAb target protein to identify regions where changes specifically impact mAb binding or activity, and subsequent analyses and surveillance can focus on these regions.
- Sponsors should characterize the epitopes to which mAb products bind to enable identification of polymorphisms, which may affect binding, and to inform decisions regarding mAb products planned for use in a combination therapy.
- Sponsors should monitor SARS-CoV-2 genomic databases continually for emerging SARS-CoV-2 variants and should evaluate phenotypically any specific variants that are prevalent or becoming prevalent that harbor substitutions in or near (<5 Å) the target

¹⁷ See the guidance for industry *Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use* (February 1997).

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epitope. Sponsors should conduct a more thorough analysis to include other substitutions at the same amino acid positions.

- Sponsors should characterize mAb products with respect to epitope binding (affinity equilibrium dissociation constant (K_D) and noncompetitive binding for combinations). Sponsors should characterize the mechanism of action for SARS-CoV-2 neutralization (e.g., blocking spike protein/receptor binding domain interaction with ACE2).
- Sponsors should determine the neutralizing activity (half maximal effective concentration (EC_{50}) value) of investigational mAb products, individually and if applicable in combination, against an array of circulating variants representing the diversity of the target protein and epitope to which the mAb binds.
- Sponsors should assess for the potential of antibody dependent enhancement (ADE). Cell culture ADE studies should assess for enhancement at concentrations that range from 125-fold below the EC_{50} value to 10-fold above the EC_{50} value of the mAb.
- Sponsors should characterize the Fc-mediated antibody effector functions of investigational mAb products, individually if part of a combination, using Fc receptor binding assays and in cell culture systems with appropriate effector molecule readouts.
- Sponsors should evaluate the neutralizing activity of mAbs, individually and if applicable in combination, against SARS-CoV-2 variants or pseudotyped virus-like particles harboring substitutions known to confer reduced susceptibility to other authorized or approved antibody products targeting SARS-CoV-2 infectivity. Activity against pseudotyped virus-like particles is useful for expediency with respect to arising variants, but ultimately activity against authentic viruses should be determined.
- SARS-CoV-2 or recombinant vesicular stomatitis virus expressing spike protein should be serially passaged in cell culture in the presence of the mAb product, individually and if applicable in combination, to select for resistant variants to understand the potential risk and nature of treatment-emergent resistance. Sponsors should characterize genotypically and phenotypically the variants selected in this manner.
- Sponsors should assess the potential for cross-resistance between novel mAb products and approved or authorized mAb products, for example, by assessing the effect of resistance-associated substitutions for a novel mAb on the activity of approved or authorized mAbs in cell culture studies using recombinant viruses or virus-like particles.
- Clinical protocols should include detailed plans to (1) characterize the impact of SARS-CoV-2 genetic variability on clinical and virologic outcomes (i.e., baseline resistance analyses) and (2) identify SARS-CoV-2 genetic changes associated with treatment (i.e., treatment-emergent resistance analyses).

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- Sponsors should consult appropriate biosafety guidelines when conducting virology studies.¹⁸
- Sponsors should also reference the guidance for industry *COVID-19: Developing Drugs and Biological Products for Treatment or Prevention* (November 2023) and the guidance for industry *Antiviral Product Development — Conducting and Submitting Virology Studies to the Agency* (June 2006).

4. *Clinical*

Sponsors of mAb products targeting SARS-CoV-2 should consider the following clinical recommendations:

- In general, sponsors should design mAb product development programs evaluating the treatment or prevention of COVID-19 to assess the effect of investigational products on clinically meaningful aspects of the disease.¹⁹
- Sponsors considering the use of a surrogate endpoint (e.g., neutralizing antibody titers) to support an EUA in situations where viral variants have affected the efficacy of currently authorized or approved therapeutic (treatment or prevention) options should seek early input from the Agency on their proposals.
- Sponsors should scientifically justify the selection of doses and regimens for phase 3 trials and discuss with the Agency. For example, results from a phase 2 dose-finding study can directly support the selection of doses and regimens for phase 3 trials.
- The size and composition of the safety database needed to support an EUA will depend on factors such as the mAb product's proposed use, the proposed patient population, and the extent and nature of the prior clinical experience with the product and with related products.
- Sponsors should also reference the guidance for industry *COVID-19: Developing Drugs and Biological Products for Treatment or Prevention* for additional recommendations on trial populations, trial design, efficacy endpoints, safety, and statistical considerations.

¹⁸ For biosafety considerations from NIH, see the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules and the FAQs — Interim Laboratory Biosafety Guidance for Research with SARS-CoV-2 and IBC Requirements under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, available at https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf. See also the Centers for Disease Control and Prevention's and the National Institutes of Health's guideline Biosafety in Microbiological and Biomedical Laboratories, available at <https://www.cdc.gov/labs/BMBL.html>. Studies should also follow applicable federal policies and guidelines related to dual use research of concern, available at <https://www.phe.gov/s3/dualuse/Pages/default.aspx>.

¹⁹ See the guidance for industry *COVID-19: Developing Drugs and Biological Products for Treatment or Prevention*.